Revised Synopsis on

Development of Computer Assisted Detection Technique for Malaria Parasite using Blood Smear Images

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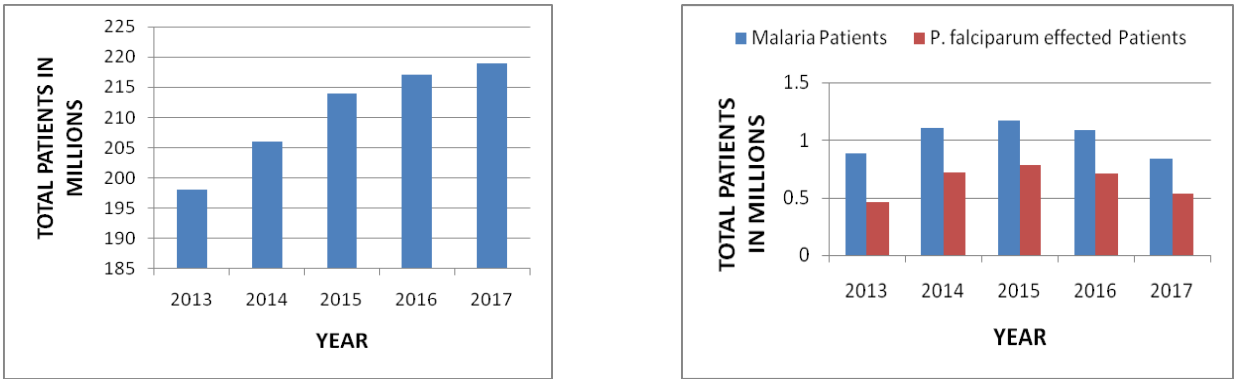
1. Introduction

Malaria has turned into a major risk and danger to the individuals all over the world as the major reason of causalities across the world is malaria. It is a life threatening but curable infectious disease which is caused by protozoan parasite. Protozoan parasite is the genus of plasmodium. Malaria disease is caused in human body through transmitted plasmodium parasite by biting of female Anopheles mosquito. Main victims of malaria are children between the ages of 0 to 5 years. It is a disease that is found in hundreds of different countries around the world. As per latest report of World Health Organization (WHO) in 2017, 219 million cases of malaria were detected in 87 countries and causalities reached to 435000 [1]. It is very common disease in Africa. In 2017, Africa was the only continent where 92% of malaria cases were detected and mortality rate was 93%. Maximum cases of malaria occur in rural areas of Africa where numbers of hospitals are very less and medical facilities are very poor and peoples are not able to afford medical facilities. Every year estimated US$ 3.1 billion is required for malaria control and elimination [1]. But the available funding is very less according to the requirement. In 2016, about 1.09 million new cases and in 2017, 0.84 million cases having malaria have been registered in India. In which, most of malaria cases were P.falciparum species affected [2].



(a) (b)

Figure 1. Year wise prevalence count of malaria patients: (a) Worldwide (b) India [1, 2]

Pattern of total worldwide malaria patients shown in **figure 1(a)** and pattern of total malaria patients and P.facliparum species affected malaria patients in India over last five years shown in **figure 1(b)**. These statistics which are very troubling can be reduced by detecting parasites and diagnosis in the early stages and it would be very helpful when expert hands are not available.

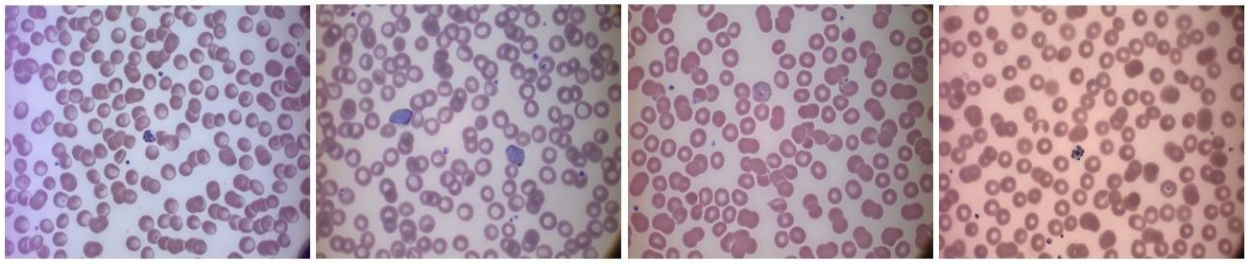
1.1 Pathology

Transmission of malaria in human body by mosquitoes was first discovered by Dr. Ronald Ross in 1897 [3]. He was a British doctor and on he was doing his research in India. For his discovery and work for prevention of malaria he won the Nobel Prize. One of the main reasons of malaria is protozoan parasite. It is the genus of plasmodium which infects Red blood cells (RBC) of human body causes the malaria [4]. Generally, female Anopheles mosquitoes and human beings are the two main hosts those are infected by the parasite. When female Anopheles mosquitoes want to nurture their eggs then they pick up the blood from human body by biting. If that person is infected by parasite then that same infected parasite blood found in the mosquito and that parasite reproduce and develop in mosquito body. When that infected mosquito bites to another person then parasites contained salivary gland are transferred into the blood of that person [5]. After transferring of parasites into human body by mosquito, malaria parasites grow with very high speed in the liver and red blood cells of that infected person. Malaria symptoms appear after a one or two weeks. Basic symptoms that appear are headache, vomiting, fever and chills. If malaria is not treated early and properly then it is very harmful for human body. It may be a reason of kidney failure, low blood sugar, respiratory distress, enlargement of the spleen etc [6]. Malaria can kill a person by destroying their red blood cells. It is a very dangerous disease for

children under the age of 5 years. Malaria during pregnancy is the one of the reason of abortion [7].

1.2 Malaria Parasites: Species and Life stages

There are five different species of protozoan parasite and these are the main cause of malaria in human body. These are Plasmodium falciparum (P.falciparum), Plasmodium vivax (P.vivax), Plasmodium ovale (P.ovale), Plasmodium malariae (P.malariae) and Plasmodium knowlesi (P.knowlesi). Among all five species first four are most common species and these species occurs in human body. Fifth species is P.knowlesi mostly occurs in monkeys lives in South - East Asia forests. But, in past years, some cases of P.knowlesi malaria occurred in human body. Most common species that found in human body is P.vivax but most dangerous species is P.falciparum [8]. All species of protozoan parasites are morphological different. On every stage of its lifecycle each species undergoes a change in its size, color, shape and morphology etc. These different stages of every species are ring, trophozoite, schizont and gametocyte [4]. Figure 2 shown the most common malaria affected blood smear images found in human body.



(a) (b) (c) (d)

Figure 2. Different types of malaria affected blood smear images

(a) P.falciparum (b) P.vivax (c) P.ovale (d) P.malariae [9]

The malaria parasite is carried by female Anopheles mosquito which acts as a vector that injects the immature form of the parasite called sporozoites into the blood stream of humans while

feeding on blood. The blood carries the sporozoites to the liver where they mature through forms of schizonts to merozoites. The merozoites are released to the bloodstream where they invade the RBCs and eventually rupture them. The merozoites multiply asexually through stages of ring trophozoites, trophozoites to schizonts which will eventually be released as merozoites to invade more RBCs. Alternatively some of them develop to sexual forms called gametocytes.

Once a non-infected mosquito has a blood meal from an infected person, the gametocyte enters the mosquito gut where they mate and produce sporozoites which in turn will cause further transmission of the disease. The intervals between the release of each generation of merozoite to the blood stream to invade RBCs is usually 48 to 72 hours and is responsible for the recurrent symptomatic attacks of chills and fever in the host [10].

1.3 Malaria Diagnosis Methods

Malaria is a very dangerous disease and one of the main reason of high mortality rate increasing every year. Main reason of large number of deaths is late detection of malaria parasites in human body. If malaria parasites in human body can detect in early stages then survival rate can be increased. In medical science, there are two main methods to detect malaria: (i) Microscopic thick and thin blood smears examination (ii) Rapid Diagnosis Test (RDT).

1.3.1 Microscopic thick and thin blood smears examination

In this, a lab examination is performed in which a blood sample is taken from a patient and then that blood sample is place on a slide. The blood sample is stained with a contrasting agent to help highlight malaria parasites in RBC.

After that, this blood sample is divided into two parts on the slide. One is called thick blood smear and another is thin blood smear. Now, a clinician examines that slide under the microscope and clinician manually counts the number of affected red blood cells. Thick blood smear helps clinicians to detect the presence of malaria parasites and thin blood smear helps to identify the species of the parasites causing the malaria. This technique to detect the malaria is a gold standard in medical field. Microscopic thick and thin blood smears examinations technique accuracy totally depends on clinician's experience. To detect and diagnose malaria through microscope a clinician may have to count more than 5000 cells manually which is an extremely tedious and time consuming task [11].

Figure 3. Microscopic thick and thin blood smears examination [12]

1.3.2 Rapid Diagnosis Test (RDT)

Rapid diagnosis test or Antigen test is a small kit that is easily available in the market in the form of kit to detect antigens derived from the malaria parasites. It is helpful for remote or rural areas where microscopic labs are less or not available. To identify the malaria a drop of blood is inserted into kit from the given hole and internally this device performs the tests and provides the result in minimum time. This type of kit is faster than manually cells counting techniques but the results of these techniques are less accurate [13].

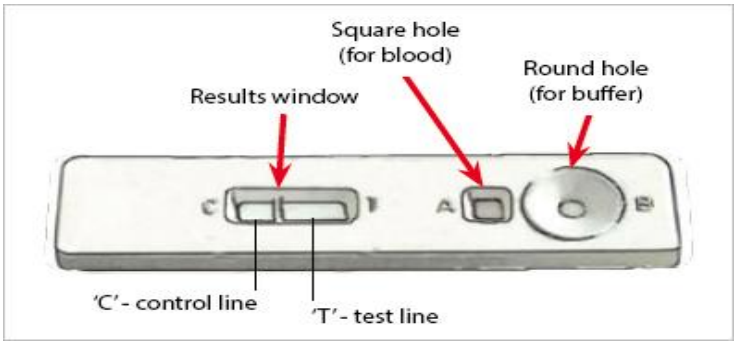


Figure 4. Rapid Diagnosis Testing (RDT) Kit [14]

2. Literature Review

Detection of malaria parasites from blood smear digital images comprises of different stages of image processing techniques. Different peer groups of researchers worked on different stages in order to detect the malaria parasites from blood smear images. These image processing tasks to detect malaria parasites from blood smear image are (i) Image acquisition and pre-processing (ii) Segmentation (iii) Feature Extraction and Selection (iv) Classification [15].

2.1 Image acquisition and pre-processing

Digital images of blood samples are required to detect that a patient is affected by malaria or not using image processing and machine learning techniques. These digital blood smear images are

collected by different sources. Collection of digital blood smear images is called image acquisition. Digital blood smear images are taken by a digital camera that is attached by digital light microscope. When blood smear images are taken by digital camera attached with light microscope, the images are corrupted by noise & thus visualization of the images is not good. So to remove that unwanted noise from images, certain pre-processing techniques have been used. Pre-processing techniques remove the noise from image for better visualization that is very useful for further analysis [16].

Different researchers used multiple pre-processing techniques for enhancing the quality of digital images. May et al. has given an approach in which median filter technique for removing the impulse noise from digital images and for removing additive noise has been used [17]. Gaussian filter is used by Arco et al. to enhance the quality of the images those are affected by Gaussian noise. Geometric mean filter is also used by Das et al. for preserving the edges and removing Gaussian noise from the digital microscopic image [18]. Laplacian filter is used by Savkare et al. for smoothening and enhancing edges of malaria parasite images [19]. To preserve the structure of an image Susan filter is suggested by Soni et al. [20]. To remove the intensity of high frequency from a digital image, low pass filter has been suggested by Diaz et al. [21]. Histogram matching technique is used by Abbas et al. to normalize the intensity value of digital image pixels [22].

2.2 Segmentation

Segmentation of blood smear images is ubiquitous need of digital pathology. It is the process in which digital images are disjoint into non overlapping regions. Each disjoint image is typically corresponds to other part of image object. Once each object of digital image is isolated, then each

object can be easily measured and classified. In literature, there are different segmentation techniques which have been applied on digital blood smear images to detect ROI (Region of Interest).

Das et al developed an automated system for classification of malaria different stages. In their research work for segmentation of thin blood smear digital images, researcher used watershed segmentation technique and this technique which provided better results for detecting erythrocytes from the whole blood smear image [18]. Further, watershed algorithm is suggested by Savkare et al. to find overlapped cells on connected components [19]. To detect ROI objects Soniet et al. used granulometry technique [20].

Makkapati et al. developed a technique for segmentation of malaria parasites in blood smear images [23]. Developed technique is used to segment red blood cells and parasites using HSV (Hue, Saturation, Value) color space. This technique segmented the red blood cells and parasites from blood smear image on the bases of hue range and optimal saturation thresholds.

Mandal et al. introduced a normalized cut method for segmentation of microscopic blood smear images. The segmentation algorithm has been used on different color spaces for finding optimal performance of digital blood smear images [24]. Result of normalized cut segmentation algorithm is good in HSV color space.

Nasir et al. proposed a segmentation based approach using K-means clustering algorithm for segmentation of malaria parasite blood smear images on 100 digital blood smear images dataset [25]. Panchbhai et al. presented RGB color space model and Otsu algorithm for RBC and parasite segmentation from 20 thin blood smear images [26].

For segmentation of microscopic blood cells digital images, Savkare et al. suggested K-mean clustering and global threshold techniques for blood cell segmentations from microscopic blood images. In this, 78 microscopic blood cell digital images are used for segmentation [27]. Najeed et al. also used K-means clustering (unsupervised approach) for the segmentation of 118 blood smear images to identify malaria parasite tissues [28].

Ma et al. introduced circle hough transformation method to detect the accurate radius of erythrocyte [29]. Khan et al. suggested K-means clustering technique for segmentation of red blood cell in digital image [30]. Otsu thresholding clustering based method is presented by Makkapati et al. to get the image mask of binary image [31]. To segment the red blood cells Chayadevi et al. used fuzzy rule based algorithm [32].

2.3 Feature Extraction and Selection

Feature extraction after segmentation is a pre requirement for feature selection and classification. The objective of feature extraction is to recognize and characterize an object whose dimensions are very nearest or similar for objects in the same class, and different for objects those are from different class. It reduces the computational complexity of the other processes and provides accurate and reliable recognition to unknown unrecognized data.

To develop a good classification model, a good feature selection method plays a very important role. Classification model processing time and results of classification model totally depends on selection and type of number of selected features or attributes. In literature, number of researchers have developed and used different feature selection methods.

To extract the features of haralick textures mean, entropy, roughness, homogeneity, standard deviation Das et al. suggested grey level co-occurence matrix [18]. To extract the intensity based features Chayadevi et al. used colour channel intensity algorithm [32]. Rajaraman et al. proposed pre-trained model technique for feature extraction and detection of malaria parasites [33]. In this, pre-trained convolutional neural network including AlexNet, VGG-16, Xception, ResNet-50 and Densenet-121 are used for extracting features from infected and uninfected 27558 cell images. The developed model for feature extraction and malaria parasite detection took more than 24 hours for training and produced 95.9% accuracy for malaria parasite detection in thin blood smear images.

For identifying the texture features from a blood smear image to detect malaria parasite Chavan et al. used histogram based feature extraction method [34]. Colour histogram features extraction technique is used by Malhi et al. for identify infected erythrocyte from blood smear images [35]. Seman et al. extracted features RBC size and shape, RBC texture, parasite shape from the thin blood smear images and used these features to classify malaria parasite species [36]. For extracting the features from digital microscopic image based on morphological, Malhi et al. used granulometry algorithm [37].

2.4 Classification

Classification is a technique to identify a pattern which belongs to which class. In this literature different author developed different classification techniques to identify a patient, whether he or she is malaria affected or not. So, there are two classes to detect whether the patient is affected from malaria or not.

Vijayalakshmi et al. introduced a deep learning approach to classified infected and non - infected falciparum malaria. Introduced technique was achieved by Visual Geometry group (VGG) network and SVM. In this, 1530 malaria digital corpus images have been used for training and testing the model. In this, transfer learning approach to train the model is used, in which trained the top layer of the model and freeze the rest out of the layers approach applied. For classification of infected or non-infected falciparum malaria, proposed model obtained 93.13% accuracy [8].

For the classification of malaria infected stages from thin blood smear images Das et al. used five different classifiers to classify the malaria infected stages. These five classifiers are Naive Bayes, Logistic regression, Radial Basis Functions (RBF) neural network, Multilayer perceptron neural network and classification and regression tree. In this, 888 erythrocytes infected and non infected image dataset is used. In which 592 labelled images are used to training the classifiers and remaining are used for testing the classifiers. The experimental results shown that among all five classifiers, multilayer perceptron network has provided the better results (accuracy 96.73%) as compared to other four classifiers [18].

Mandal et al. introduced Regression based classification for identifying P.vivax parasite from blood smear images and used dataset of 37 images [24]. Seman et al. developed a Multilayer Perceptron Network (MLP) for classification of different malaria parasites species from thin blood smear images. In this work, three different species are classified from malaria parasites: P.falciparum, P.malariae and P.vivax [36]. Authors used back propagation algorithm of MLP network for training and compare results of MLP network with Lavenberg - Marquardt and

Bayesian rule algorithms. MLP network has produced the better results as compound to other two algorithms.

Otsu thresholding method is used by Malihi et al. to classify four species of malaria parasites in blood smear images. This technique has provided better results in comparison to other techniques. In this, 363 blood smear images are used and obtained 91% accuracy [37].

Further, Anggraini et al. Has been classified the different stages of malaria parasites using Bayesin classifier on 110 thin blood smear images and obtained 93.3% accuracy [38]. Kumarasamy et al. suggested SVM (Support Vector Machine) to determine the different stages of malaria parasite infection in 530 blood smear images and got 86% accuracy. Minimum distance classifier technique is proposed by Ghate et al. for detecting the presence of malaria parasites using 80 blood smear images and got 83.75% accuracy [39]. Savkare et al. presented Otsu thresholding, watershed transform and SVM binary classifier for classification of normal and parasite infected cells [40]. Das et al. proposed Bayesian approach for automated screening of malaria parasite from microscopic images [41].

Kareem et al. developed an automated technique for detection of malaria parasites in thin blood smear images. In this, dataset of more than 200 images are used. Two methods of classification for parasites detection are used. First one is based on relative size and morphology and second is based on intensity variation. Final results of developed model has shown accuracy rate of 87% [42]. Yunda et al. introduced Multi-layer perceptron algorithm for classification of gametocyte stage of P.falciparum and P.vivax of malaria species in thick blood smear images. In this, 248 thick film blood smear images are used and got 77.19% accuracy [43].

Prasad et al. presented a decision support system using morphological approach to classify the infected and non-infected malaria parasites in thin blood smear images. In this, 200 thin blood smear images have been used and 96% accuracy has been obtained [44].

Memeu et al. has given an artificial neural network based rapid malaria diagnostic method for automatic classification and detection of plasmodium parasites stages and species in thin blood smear images. For training and testing of developed model, dataset of 200 thin blood smear images are used and achieved 79.7% accuracy [45].

In this Rosado et al. developed a supervised classification technique to detect malaria parasites in thick blood smears. In this, Machine Learning (ML) classification 10-fold cross-validation for WBC (White Blood Cell) and P.falciparum trophozoites detection has been performed. The dataset of 1843 thick blood smear images has been taken by mobile devices has shown 91.8% accuracy [46].

Mohammed et al. presented a technique for detection and classification of malaria from 160 thin blood smear images taken from Centre for Disease Control and Prevention (CDC). To extract the red blood cells from blood smear images researches used morphological processing. This technique found the parasites and overlapped cells in the image. On the basis of number of red blood cells in each image, red blood cells are classified into two classes infected and non infected cells. After that, normalized cross correlation algorithm has been employed to classify the affected blood smear parasite into four different species of malaria. Proposed method produced 95% accuracy for detection [47].

In this, Bibin et al. has given an automated technique to detect malaria parasites in peripheral blood smear images. Given binary classifier is based on deep learning. 1978 images are used for training and testing of technique and achieved 96.21% accuracy [48].

Dave et al. used adaptive thresholding, erosion and dilation operations for diagnosis of malaria from 117 thin and thick blood smear microscopic digital images and got 89.88% accuracy [34]. Oliveira et al. suggested face detection algorithm to identify plasmodium parasites from blood samples. In this, dataset of 1332 blood sample images has been taken and shown 91% accuracy [49].

Mohanty et al. presented auto encoder (AE) neural network un-supervised technique to identify malaria in blood smear images. In this, AE technique has been compared with SOM technique. AE technique obtained 87.5% accuracy in comparison to 79% accuracy of SOM technique. In this, 1182 thick blood smear images have been used to performed experiments [50].

3. Justification for Research

3.1 Motivation

Malaria is the disease which has highest mortality rate as compared to other diseases. In 2016, there were 217 million cases which were detected worldwide and causalities reached to 4,45,000 due to malaria which has increased enormously in number to 219 million cases of malaria and causalities reached to 4,35,000 in the year 2017 as per WHO report [1]. Globally, Malaria is responsible for 3 to 4 million deaths per year. Out of these deaths, Malaria is the only disease which is the fourth leading cause of deaths in children of less than 5 years [51].

Malaria is presently rated as major cause of high mortality rate worldwide because of the late detection of malaria. The mortality rate of malaria can be reduced significantly by early detection and by increasing awareness in the population. Early detection and diagnosis of malaria will increase the survival rate. Therefore, to facilitate early detection and to reduce mortality rate due to malaria, an automated computer assisted technique is required for early detection of malaria with high accuracy rate.

3.2 Research Gaps

A detailed literature study regarding classification and detection of malaria in blood smear images has resulted in drawing out the following inferences which are still remain to be addressed:

Malaria has five different types of species: P.falciparum, P.vivax, P.malariae, P.ovale and P.knowlesi [4]. In literature, authors developed methods that can recognize only one type of malaria parasite [8]. But it is possible that the patient could be affected by more than one parasites species. Hence, there is a need of such a technique that can recognize different types of malaria parasites.

In medical field, microscopic thin and thick blood smear examination to detect malaria is a gold standard. This technique is a very time consuming and its accuracy completely depends on clinician's expertise to detect and diagnose malaria through microscope. A clinician may have to count more than 5000 cells manually which is an extremely tedious and time consuming task [11]. Therefore, there is a need of technique that can detect and count affected cells automatically [16].

For classification of malaria parasites from blood smear images authors trained machine with different algorithms and techniques. Training model is taking longer to learn [33]. Hence, there is a need to reduce the training time in order to train the classification models.

In literature, it has been found that all the existing state-of-art techniques used for detection of malaria from microscopic blood smear images are not very accurate and used local datasets to perform their experiments [18, 33, 46, 48]. Therefore, there is a need of automatic technique that can improve the accuracy of detection of malaria parasites.

In literature, the results obtained by authors are based on non-standard datasets. Each dataset parameters are different in terms of distinct magnification factors and separate count of number of images. Bibin et al. presented a Computer Assisted Diagnosis (CAD) system in which 1978 images of 100x and 40x magnification factors have been used [48]. Therefore, there is a need to develop a standard dataset that can be used by ML experts and expert histologists to introduce new algorithms where accuracy of classification can be improved.

In literature, authors developed the model that analyse the blood smear digital images those are taken from a camera that is attached with microscope. Hence, there is a need of a technique that can analyse thin blood smears images acquired exclusively with smart phones [52].

Inter-observer variability is a variation in between the results obtained by two or more pathologists examining the same blood sample. Intra-observer variability is the variations in results when one pathologist observing the same blood sample more than once [53]. Hence, there is a need of an automatic technique that can eliminate inter and intra observer variability to detect malaria.

Technique that is used by different authors to diagnose malaria is invasive technique. In which blood sample is taken by an injection syringe. Therefore, there is a need of non-invasive technique that can be use for detection of malaria [54, 55].

4. Problem Statement

Malaria is a life threatening disease that is a major cause of high mortality rate worldwide. Main reason of high mortality rate is late detection of malaria. High mortality rate of malaria can be decreased by detecting the malaria at an early stage. Therefore, an automated computer assisted technique is needed, which will help the pathologists to provide a second opinion for effective and early detection of malaria and reduce the mortality rate.

4.1 Objectives

Based on the inferences drawn out of the critical literature review, the objectives are as follows:

- To study the existing state-of-art techniques for the detection of malaria parasite using blood smear images.
- To segment the red blood cells for the detection of malaria parasite using blood smear images to facilitate the classification process.
- To develop a technique for the classification of parasitized and uninfected cells to aid in improved disease screening.
- To test and validate the proposed technique on the blood smear images dataset of malaria with the state of art techniques existing in literature.

4.2 Methodology

- **Literature Review** - In literature review, the reputed journals and conferences which published the research papers based on malaria detection using blood smear images had been studied. Then review the papers subsequently and extensively to find out the

prominent trends pertaining to automated detection of malaria. Further, directions will be set for future research work.

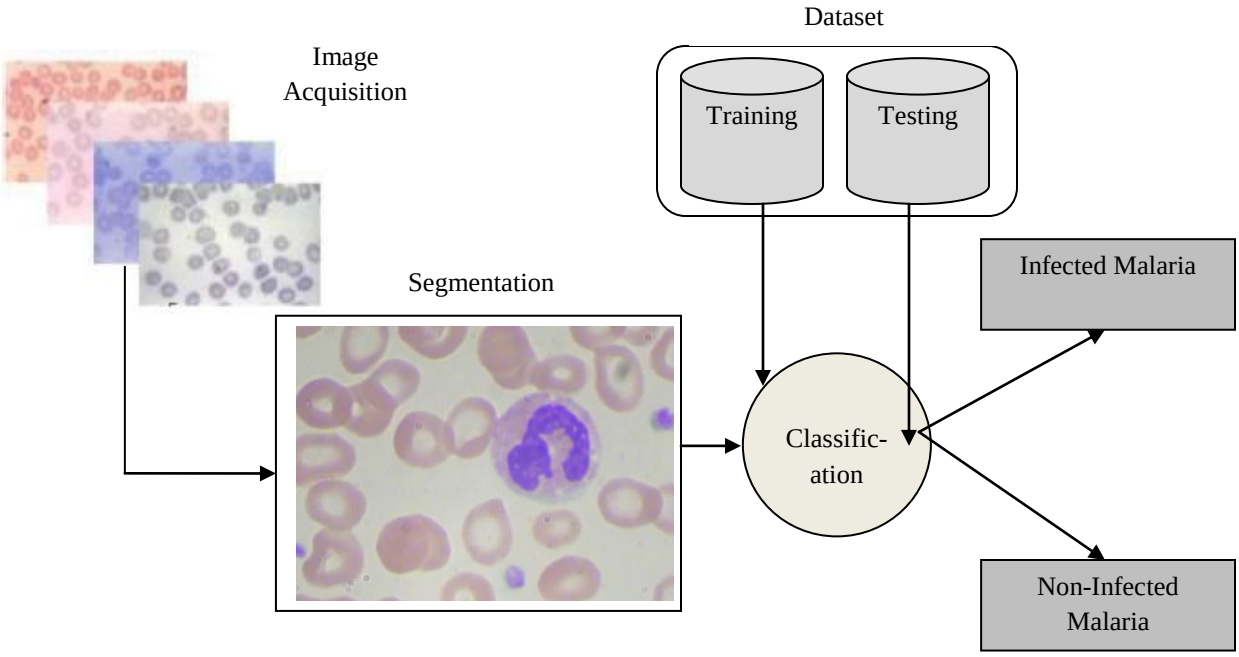


Figure 5. Flow Chart of Research Methodology for Proposed Work

- **Image Acquisition -** Numbers of malaria blood smear images datasets are publically available or blood smear images of malaria patients can be collected from hospitals or clinical laboratories for segmentation and classification.

- **Segmentation -** The objects of interest will be segmented for the detection of malaria parasite using blood smear images to facilitate the diagnostic process as shown in **figure 5**.

- **Classification -** After segmentation, a technique will be proposed to classify parasitized and uninfected cells from microscopic blood smear images. As shown in **figure 5,** Blood smear images dataset will be divided into two parts, training dataset and testing dataset. Training dataset will use to train the machine and testing dataset will use to test the blood smear images are malaria infected or not.

- **Analysis of results -** The classification results will be analysed by testing and validating the proposed technique with other state-of-art techniques on the microscopic blood smear image dataset of malaria.

5. Work Plan

The research tasks for the proposed work are tabulated quarterly as illustrated in Table 1:

Table 1. Work Plan

Tasks	(January 2018 – December 2018)				(January 2019 – December 2019)				(January 2020 – December 2020)			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Course work												
Submission of Synopsis												
To study the existing state of art techniques for the detection of malaria parasite using blood smear images.												
To segment the red blood cells for the detection of malaria parasite using blood smear images.												
To develop a technique for the classification of parasitized and uninfected cells to aid in improved disease screening.												
To test and validate the proposed technique on the blood smear images dataset of malaria with the state of art techniques existing in literature.												
Thesis preparation and manuscript writing.												

6. Expected Outcomes

It is expected that the proposed research will yield to a technique that can classify that whether the patient is malaria affected or not using digital microscopic blood smear images. The input to the technique will be a collection of blood smear images. To accomplish the objectives, segmentation of blood smear images will be performed which will identify object of interest to facilitate the classification process effectively. After the segmentation of blood smear images, the suspicious regions will be classified as malaria affected or not. Finally, to assess the effectiveness of the proposed technique, it will be compared with the other state-of-art techniques. The outcome of the proposed work will be an aid for experienced pathologists by providing a second opinion for effective and early detection of malaria in order to avoid false decisions.

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